THE BULLETIN OF
Mathematical
BIOPHYSICS

THE UNIVERSITY OF CHICAGO PRESS · CHICAGO · ILLINOIS

VOLUME 4
NUMBER 4
DEC. 1942

THE BULLETIN OF Mathematical Biophysics

EDITED BY N. RASHEVSKY

The Bulletin is devoted to publications of research in Mathematical Biophysics, as described on the inside back cover.

THE BULLETIN is published by the University of Chicago at the University of Chicago Press, 5750 Ellis Avenue, Chicago, Illinois, quarterly, in March, June, September, December. ¶The subscription price is $2.50 per year, the price of single copies is 75 cents. Orders for service of less than a full year will be charged at the single-copy rate. ¶Patrons are requested to make all remittances payable to The University of Chicago Press in postal or express money orders or bank drafts.

THE FOLLOWING are authorized agents:

For the British Empire, except North America, India, and Australasia: The Cambridge University Press, Bentley House, 200 Euston Road, London, N.W. 1. Prices of yearly subscriptions and of single copies may be had on application.

CLAIMS FOR MISSING NUMBERS should be made within the month following the regular month of publication. The publishers expect to supply missing numbers free only when losses have been sustained in transit, and when the reserve stock will permit.

BUSINESS CORRESPONDENCE should be addressed to The University of Chicago Press, Chicago, Ill.

COMMUNICATIONS FOR THE EDITOR and manuscripts should be addressed to N. RASHEVSKY, Editorial Office of the Bulletin of Mathematical Biophysics, 5822 Drexel Avenue, Chicago, Ill.

PRINTED BY THE DENTAN PRINTING CO., COLORADO SPRINGS, COLORADO

BULLETIN OF

Mathematical Biophysics

CONTENTS

AN ANALYSIS OF THE SHAPES OF A CELL DURING DIVISION WITH PARTICULAR REFERENCE TO THE ROLE OF SURFACE TENSION - - - - 151
H. D. LANDAHL

EQUILIBRIUM SHAPES IN NON-UNIFORM FIELDS OF CONCENTRATION - - - - - - - - - 155
H. D. LANDAHL

CELLULAR FORMS: THE TRI-AXIAL CELL - - - - 159
ALSTON S. HOUSEHOLDER

THE LINEAR THEORY OF NEURON NETWORKS: THE STATIC PROBLEM - - - - - - - - - 169
WALTER PITTS

SOME PROBLEMS IN MATHEMATICAL BIOPHYSICS OF VISUAL PERCEPTION AND AESTHETICS - - 177
N. RASHEVSKY

INDEX TO VOLUME FOUR - - - - - - - - - 193

VOLUME FOUR DECEMBER 1942 NUMBER FOUR

IMPORTANT ANNOUNCEMENT

The increase in the output of papers in the field of mathematical biophysics makes it difficult to insure prompt publication without an increase in the size of the journal. Therefore, the Bulletin of Mathematical Biophysics inaugurates the following service:

Upon acceptance of a paper, the Editor, if necessary, will ask the author to shorten the paper to an extent dictated by the requirements of a reasonably prompt publication. The shortening should in no case reduce the paper to a mere abstract. Such a shortened paper will be published within six months or less.

The unabbreviated original manuscript will be kept on file at the editorial office. Any person desiring to avail himself of the complete manuscript, may obtain promptly a microfilm copy of the latter, at the cost of 1¢ per page plus postage, by applying to the Editorial Office, 5822 Drexel Avenue, Chicago, Illinois.

All papers in the Bulletin which have been thus shortened, will be marked at the end by the symbol MF, followed by a figure, indicating the number of doublespaced typewritten pages of the unabbreviated manuscript.

BULLETIN OF
MATHEMATICAL BIOPHYSICS
VOLUME 4, 1942

AN ANALYSIS OF THE SHAPES OF A CELL DURING DIVISION WITH PARTICULAR REFERENCE TO THE ROLE OF SURFACE TENSION

H. D. Landahl
The University of Chicago

An expression is given for the contribution to the relative elongation by any volume element or its surface. The case in which only a constant surface tension is acting is considered in greater detail. From measurements of an egg in several stages, the empirical variation of an expression proportional to the above function is obtained. In the constricting region and near the ends of the cells, the change of shape is opposite to that which would be due to a constant surface tension alone. The effect of streaming which may arise from a variable surface tension is considered. The effect of forces which arise in this manner may be sufficient to explain the discrepancy in the constricting region if the streaming is considered due largely to such a variable surface tension.

The shape of a cell at any instant, as well as changes of shape with time, can be considered as the resultant of various volume and surface forces. If the former can be derived from a potential, one may substitute for them an equivalent surface force. The average relative change in length of the cell can be written as (Rashevsky, 1940)

$$\bar{e} = \frac{1}{r_1}\frac{dr_1}{dt} = \frac{1}{3\eta V}\int\int [zZ - \tfrac{1}{2}(xX + yY)]\, dS\,, \tag{1}$$

where $2r_1$ is the length, η is the viscosity, V the volume of the cell, X, Y and Z are the components of the total surface force given by the sum of the surface forces and the surface force equivalent of the volume forces. If we consider a figure of revolution about the z-axis, let $\rho^2 = x^2 + y^2$ and let ν be the normal to the surface at (ρ, z), then equation (1) may be written, on integrating with respect to the polar angle,

$$\frac{\delta \bar{e}}{\delta z} = \frac{2\pi}{3\eta V}\rho(zZ - \tfrac{1}{2}\rho P)\sec(\nu\rho)\,, \tag{2}$$

where P is the component of the total surface force along the ρ-axis.

The left hand member of (2) represents the contribution to average relative elongation $\bar{e}$, by the surface of the element between z and $z + \delta z$. Its value can be measured for any z at a particular time, so that $Z(P)$ could be determined. This gives little information about

Z and P, which themselves are composite surface force components. We shall instead consider the component of $\delta\bar{e}/\delta z$ is due to a surface tension, γ, which has a constant value over the surface. If R_1 and R_2 are the principle radii of curvature and R twice their harmonic average, then that part of $\delta\bar{e}/\delta z$ due to this factor may be written

$$\frac{\delta\bar{e}}{\delta z} = -\frac{2\pi\gamma}{3\eta V}\frac{\rho}{R}\left[z \tan(\nu\rho) - \tfrac{1}{2}\rho\right] = \frac{2\pi\gamma}{3\eta V}\phi(z)\,, \tag{3}$$

where $\phi(z)$ is defined by this equation and is a function of z since the shape determines $\rho(z)$. The function $\phi(z)$ can be determined empirically for any given shape by measuring ρ, R_1, R_2 and $\tan(\nu\rho)$ for any z. The empirical expression for $\phi(z)$ may give some insight into the role played by surface tension. For this reason, enlarged photographs of three successive stages of an *Arbacia* egg, denuded by treatment with KCl, were measured to determine $\phi(z)$ as shown in Figure 1. The photographs were obtained through the courtesy of Dr. R. Buchsbaum. Each point is obtained from measurements of the egg. The curves correspond to the tracing of the shapes correspondingly numbered in the figure. The time between stages is half a minute. The curves, which are free hand drawings through the points, are stopped at the end point of the cell along the elongation axis. The value of ϕ at the end of the cell is obtained from measurements and the limit of ρ tan $(\nu\rho)$ is obtained analytically by assuming that the end is approximated by part of a sphere. The area under the positive part of each curve is very nearly equal to the total area under the negative parts. From the curves, we see that the effect of a true surface tension for these shapes is such that in the region of the neck the tendency is to reduce elongation, and thus to reduce constriction. The effect becomes progressively greater with time. Evidently some other surface or volume force than a surface tension must be acting here to cause constriction. In the middle range, from about $.5\times10^{-3}$ to 3×10^{-3} cm., the effect of surface tension is such as to produce an elongation. This effect, as measured by the area under the positive part of the curves, is much the same in successive shapes, perhaps decreasing with time. If so, the change in shape in this region is as expected from a surface tension. The part of the curve near the end shows the existence of a tendency to reduce elongation. A comparison of the areas under the curves indicates that the tendency to oppose elongation becomes greater with succeeding shapes. Thus the shape in this region is changing in the wrong way from that expected by a surface tension. Thus it is probable that the effect of volume forces and surface forces, other than that due to a constant surface tension, must be such that, in the neck region and near the ends, the contribution towards elongation will be positive.

The variation of surface tension from pole to equator has been suggested as a factor in cell division (Spek, 1918, cf. also Wilson, 1925). It should be noted that a variation of the surface tension with z would not greatly affect the above argument as such variations of force could be sustained by the outside medium. However, this is perhaps not probable. It is more likely that variations of surface tension would be sustained largely by streamings set up in the cell. In general, such streamings are observed. One might attempt to compute the magnitude of the velocity of the streaming necessary to sustain the variations required to make the net elongation positive, or, using the observed order of magnitude of such streamings, to obtain the effective volume force in the neck region and see whether this could overbalance the negative effect of surface tension.

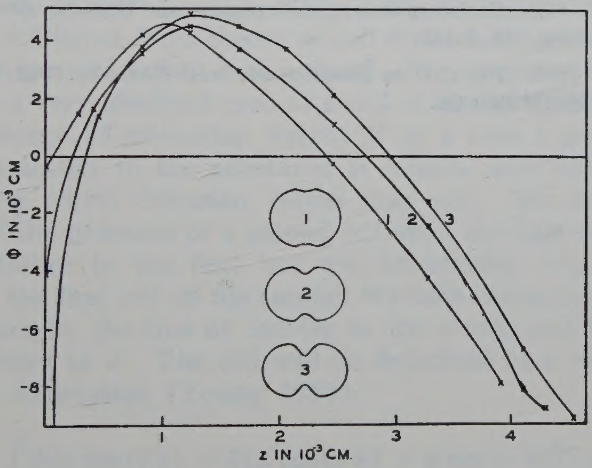

FIGURE 1

Consider the case of the shape II of Figure 1. The average of ϕ in the neck region in which $\phi < 0$ is $\bar{\phi} = -1.4\times10^{-3}$ cm. If we use $\gamma \sim 10^{-1}$ dynes cm.$^{-1}$, the average value of $\delta\bar{e}/\delta z$, in this region, due to surface tension is $-.5/\eta$ sec.$^{-1}$. The contribution to $\delta\bar{e}/\delta z$ for this region due to streaming, which we assume to be due only to the variable surface tension, may be estimated in the following manner. If the velocity of streaming in this region, is assumed to be $\sim 10^{-3}$ cm. sec.$^{-1}$, falls off to a negligible value in a distance, $d \sim 3\times10^{-4}$ cm., or about one-half the width of the neck, so that $d = z$ for $\phi = 0$, then the force per unit area is $\eta v/d$. The area upon which this is acting is of the order of πr^2, where r is the radius of the neck. This force is equivalent, in order of magnitude, to a pressure on the surface of the neck, in the region where $\phi < 0$, of $\pi r^2 \eta v/(d\pi rd)$. Dividing this pressure by 3η we obtain for the contribution to $\delta\bar{e}/\delta z$ in this region due to the streaming, the value $rv/(3d^2) \sim 10$ sec.$^{-1}$ We have considered the pressure to be of the order of magnitude, of the pressure difference. Comparing this value with that for surface tension alone, and giving η a value of 10^{-1} poise, we see that the latter could be an important factor at this particular stage. In this illustration we may have underestimated the former and overestimated the latter. It may be noted that the effect of the viscosity does not enter the resulting expression for the contribution to the relative elongation rate due to streaming.

LITERATURE

Rashevsky, N. 1940. *Advances and Applications of Mathematical Biology.* Chicago: The University of Chicago Press.

Spek, J. 1918. "Oberflachenspannungsdifferenzen als Ursache der Zellteilung." *Arch. f. Entwm.* 44, 5-113.

Wilson, E. B. 1925. *The Cell in Development and Heredity.* 3rd Edition. New York: The MacMillan Co.

BULLETIN OF
MATHEMATICAL BIOPHYSICS
VOLUME 4, 1942

EQUILIBRIUM SHAPES IN NON-UNIFORM FIELDS OF CONCENTRATION

H. D. LANDAHL
THE UNIVERSITY OF CHICAGO

The special case of a metabolizing cell, with infinite permeability, suspended in the field of an equivalent cell is treated exactly to determine its equilibrium shape for small deformations. It is found that flattening takes place along the line of centers.

In the early cleavages of an egg, the cleavage plane generally depends upon the relative position of the particular blastomere. On the basis of the diffusion force theory of cell division (Rashevsky, 1940), one would in general expect such a result. For the present we confine ourselves to a very idealized case of a cell of radius r_0 which metabolizes a substance of molecular weight M at a rate q gm cm^{-3} sec^{-1}, whose permeability to the substance is infinite and which contains structures on which diffusion forces may act. We consider first the effect of the presence of a second cell upon the first cell when the second is similar to the first but not deformable, i.e., we neglect the effect of the first cell on the second. We take the center of the first cell as the origin, the line of centers as the z-axis and the distance between centers as d. The cell will be deformed at a rate which is given by the expression (Young, 1939)

$$\bar{e} = \int_S \int \Phi\{z \cos(\nu z) - \tfrac{1}{2}[x \cos(\nu x) + y \cos(\nu y)]\}\, dS \qquad (1)$$

where

$$\Phi = -RT\mu c / 2\eta_1 M V_1 ; \qquad (2)$$

c is the concentration of the metabolite, η_1 is the viscosity of the cell, V_1 its volume, and μ is a measure of the relative volume of particles in the cell. Actually the expression for Φ is more complicated than given above (Landahl, 1942a), and the above is correct only as to order of magnitude when the particles, upon which the force is acting, are small.

In addition to the deforming force, there will be a repulsion between the cells. We shall not consider this effect for the present.

Introducing spherical coordinates, r, θ and φ, and setting $\xi = \cos\theta$, equation (1) becomes

$$\bar{e} = \int_0^{2\pi} \int_{-1}^{1} \Phi\, r'^3 P_2(\xi)\, d\xi d\varphi\,, \tag{3}$$

where $P_2(\xi)$ is the second Legendre polynomial and r' is the value of r at the surface of the cell. We shall consider only very small deformations, so that we may set $r' = r_{01}$.

The concentration due to the first cell at P can be expressed by

$$c_1(P) = \frac{1}{4\pi D_e} \int\int\int \frac{q_1\, dV}{\rho_1} \tag{4}$$

where D_e is the external diffusion coefficient, ρ_1 is the distance from the element dV to the point P, and the index 1 refers to the first cell. Since we are considering only very small deformations from the spherical shape, we have

$$c_1(P) = q_1 V_1 / 4\pi D_e r_1\,. \tag{5}$$

Similarly for the second cell we have

$$c_2(P) = q_2 V_2 / 4\pi D_e r_2 \tag{6}$$

where r_2 is the distance from the center of the second cell to the point P. But if $H(\xi, r/d)$ is the generating function for the Legendre polynomials, then (6) may be written

$$c_2(P) = \frac{q_2 V_2 H\left(\xi, \frac{r_{01}}{d}\right)}{4\pi D_e d}. \tag{7}$$

Introducing $c = c_1 + c_2$ into (2) and (3), we obtain

$$\bar{e} = -\frac{1}{2\pi} \int_0^{2\pi} \int_{-1}^{1} \left[\frac{K_1}{r_{01}} + \frac{K_2 \eta_2}{d\, \eta_1} H\left(\xi, \frac{r_{01}}{d}\right)\right] P_2(\xi)\, d\xi\, d\varphi\,, \tag{8}$$

or

$$\bar{e} = -\frac{2r^2_{01}\, \eta_2 K_2}{5\, \eta_1 d^3}\,, \tag{9}$$

where Rashevsky (1940)

$$K = R\, T\, q\, \mu\, r^3_0 / 4\, M\, \eta\, D_e\,. \tag{10}$$

If γ_1 is the surface tension of cell one, we have the contribution to $\bar{e}$, due to this force, the amount (Young, 1939)

$$-\frac{\gamma_1}{2\,\eta_1} \frac{(r_1 - r_2)}{r_1 r_2}\,, \tag{11}$$

where a coefficient which varies from slightly greater than unity to slightly less, as r_1/r_2 varies from 1 to ∞, is neglected. Thus setting the sum of these terms equal to zero we have the equilibrium deformation. Here $2r_1$ and $2r_2$ are the length and width of deformed cell 1. If

$$\varepsilon = (r_1 - r_{01})/r_{01} \tag{12}$$

we have, on neglecting powers of ε greater than the first,

$$\varepsilon = -8\,\eta_2\,r^3_{01}\,K_2/15\,\gamma_1\,d^3\,. \tag{13}$$

Thus since ε is negative, cell one is compressed in the direction of the line of centers.

If the parameters of the cells are identical, the maximum value of ε, ε_m, is given when $d = 2r_0$, or

$$\varepsilon_m = -K\,\eta/15\,\gamma\,. \tag{14}$$

For dividing *Arbacia* eggs $K\eta/\gamma$ turns out to be about 2/3 (Landahl, 1942b). Thus ε_m is of the order of five per cent for this case. For eggs not about to divide the value of $K\eta/\gamma$ has not been estimated, but if this turned out to be about one per cent or less, it would be very difficult to detect such an effect because of difficulties of measurement. However, a much smaller effect might be ample to determine the direction in which the cell will elongate if this effect takes place at a proper stage. Thus generally the cleavage of two daughter cells is in the direction as required by the above considerations.

If we pass to the case in which there are four cells whose centers form a square, each cell touching two others, we can determine that the plane of cleavage would be in the plane of the cells, as is generally the case.

From the method of images we would predict that there should be a flattening effect, in addition to gravity, when a cell rests upon an impermeable plane, while a cell at the intersection of two planes should elongate in the direction of the line of intersection of the planes. Such effects could show up in the predominance of the orientation of the cleavage planes in the proper directions.

In the above development, we have assumed an infinite permeability, and thus the effect from one cell to the next may be greatly different in magnitude from that predicted above, though in the same direction. For this reason, the estimates of magnitude are little more than illustrations.

In view of equation (3), we may determine $\bar{e}$ for rather general fields of concentration. Let the field be independent of φ. The concentration, and thus Φ of equation (2), is given by a sum of spherical harmonics. If Φ is thus expressed, and A_n and B_n are coefficients of the harmonics of degree n and $(-n-1)$, then we have from equation (3),

$$\bar{e} = \frac{3}{5} V_1 (A_2 r^{-3}_{01} + B_2 r^{2}_{01}) \qquad (15)$$

for very small deformations. At equilibrium the deformation is then obtained in a manner similar to that used in deriving equation (13). Thus, for small deformations, a knowledge of A_2 and B_2 is sufficient to determine the effect of the concentration field.

This work was aided in part by a grant from the Dr. Wallace C. and Clara A. Abbott Memorial Fund of the University of Chicago.

LITERATURE

Landahl, H. D. 1942. "A Kinetic Theory of Diffusion Forces in Metabolizing Systems." *Bull. Math. Biophysics*, 4, 15-26.

Landahl, H. D. 1942. "A Mathematical Analysis of Elongation and Constriction in Cell Division." *Bull. Math. Biophysics*, 4, 45-62.

Rashevsky, N. 1940. *Advances and Applications of Mathematical Biology.* Chicago: The University of Chicago Press.

Young, G. 1939. "On the Mechanics of Viscous Bodies and Elongation in Ellipsoidal Cells." *Bull. Math. Biophysics*, 1, 31-46.

BULLETIN OF
MATHEMATICAL BIOPHYSICS
VOLUME 4, 1942

CELLULAR FORMS: THE TRI-AXIAL CELL. I

ALSTON S. HOUSEHOLDER
THE UNIVERSITY OF CHICAGO

Without assuming a spheroidal shape for the cell, more general approximate deformation equations are derived which allow for non-uniformities in the external diffusion field and within the cell itself. It is found that in the absence of such non-uniformities, however, the only stable shapes are those in which the cell is spheroidal. Moreover, in conformity with previous results derived by somewhat different approximations, it is found that the spherical equilibrium is always stable and the approach monotonic unless, for a sufficiently large volume or a sufficiently high metabolic rate, there exist two non-spherical equilibria, one of prolate type and one of oblate type.

1. *The diffusion equation.* Rashevsky's discussion of diffusion in the cell, of cell division, and, more generally, of cellular forms (1940, chapters i, iii and v) presupposes the cell to be roughly spheroidal in shape. He thus ascertains the conditions under which the cell will be either oblate, prolate, or spherical. The present object is, essentially, to carry out the same calculations without, however, making the spheroidal assumption, and so to determine the more general equilibrium shape, i.e., its diameter along each of three perpendicular directions. The further possibility is also allowed that the external diffusion field has been rendered unsymmetric—say by neighboring cells unsymmetrically placed, or by other means. This is a possibility considered by Williamson in a forthcoming paper, but with Rashevsky's assumptions of symmetry.

In attempting to approximate in the usual fashion we must revise somewhat the details of the geometric picture. Instead of approximating the cell shape by a spheroid or by a cylinder with spherical caps, we must now approximate it by a rectangular parallelepiped of dimensions $2r_1 \times 2r_2 \times 2r_3$. There are six faces to the cell and we may denote by the subscript pairs $(j1)$ and $(j2)$ $(j = 1, 2, 3)$ the two faces normal to the j-th axis. We may then, as usual, let c_{j1} and c_{j2} be the concentrations just inside, c'_{j1} and c'_{j2} the concentrations just outside the corresponding faces.

In deriving the approximate diffusion equations Rashevsky introduces the quantity δ to characterize the external diffusion field. This is the distance from the cell membrane at which, if the concentration gradient were constant, the concentration would fall to the value c_0 which it has at infinity. Rashevsky supposes δ to be the same on all sides of the cell. We shall remove this restriction. Moreover, Rashevsky supposes that the "average" value of the internal concentration is at a point halfway from center to periphery. We shall leave unspecified this point of average concentration and say only that $\alpha_{j1}r_j$ or $\alpha_{j2}r_j$ represents the distance from the center to the face $(j1)$ or $(j2)$ at which this average concentration occurs. With this understanding we may write in the usual way

$$D_i \frac{\bar{c} - c_{j\sigma}}{\alpha_{j\sigma}\, r_j} = h(c_{j\sigma} - c'_{j\sigma}) = D_e \frac{c'_{j\sigma} - c_0}{\delta_{j\sigma}}, \quad (\sigma = 1, 2; j = 1, 2, 3), \tag{1}$$

thus assuming the principal diffusion directions to be outward.

If we set

$$c = \bar{c} - c_0 , \tag{2}$$

then we can solve the equations (1) for $c_{j\sigma}$ and $c'_{j\sigma}$:

$$\begin{aligned} c'_{j\sigma} &= c_0 + \left(1 + \frac{D_e}{h\,\delta_{j\sigma}} + \frac{\alpha_{j\sigma}\, r_j}{D_i}\frac{D_e}{\delta_{j\sigma}}\right)^{-1} c , \\ c_{j\sigma} &= c_0 + \left(1 + \frac{D_e}{h\,\delta_{j\sigma}}\right)\left(1 + \frac{D_e}{h\,\delta_{j\sigma}} + \frac{\alpha_{j\sigma}\, r_j}{D_i}\frac{D_e}{\delta_{j\sigma}}\right)^{-1} c . \end{aligned} \tag{3}$$

In each second there passes through the face $(j\sigma)$ the amount

$$4r_k r_l h(c_{j\sigma} - c'_{j\sigma}) = 4r_k r_l \frac{D_e}{\delta_{j\sigma}}\left(1 + \frac{D_e}{h\,\delta_{j\sigma}} + \frac{\alpha_{j\sigma}\, r_j}{D_i}\frac{D_e}{\delta_{j\sigma}}\right)^{-1} c , \tag{4}$$

whereas the total production within the cell in one second amounts to $8qr_1r_2r_3$, and the increase in the amount of metabolite within the cell is $8r_1r_2r_3\, dc/dt$. Hence

$$\frac{dc}{dt} = q - \tfrac{1}{2}hc\Sigma\left(1 + \frac{h\,\delta_{j\sigma}}{D_e} + \frac{h\,\alpha_{j\sigma}\, r_j}{D_i}\right)^{-1} r_j^{-1}. \tag{5}$$

The coefficient of c in this equation is the value of Λ^{-1}, the reciprocal of Rashevsky's "diffusion resistance" for this case. For constant r, the equation is again linear in c and requires no discussion. We turn therefore to the deformation equation.

2. *The deformation equations.* The derivation of these equations (Rashevsky 1940, chap. iii) requires the evaluation of three surface integrals, each of six terms having the same form except for constant multipliers. The first integral, describing the effect of the

volume diffusion forces, consists of terms of the type

$$c_{j\sigma} r_j S_{j\sigma} = 4r_1 r_2 r_3 c_{j\sigma} = \tfrac{1}{2} V c_{j\sigma} ,$$

with a constant multiplier. Since the entire integral involves also the terms

$$-\tfrac{1}{4} V (c_{k\sigma} + c_{e\sigma}),$$

it is legitimate, and convenient, to replace each $c_{j\sigma}$ by $c_{j\sigma} - c_0$.

The second integral describes the effect of the osmotic forces and a typical term is

$$r_j X_{j\sigma} S_{j\sigma} ,$$

where $X_{j\sigma}$ is the component of the osmotic pressure. But this pressure has the direction of the normal and it is proportional, at the face $S_{j\sigma}$, to $c_{j\sigma} - c'_{j\sigma} = (c_{j\sigma} - c_0) - (c'_{j\sigma} - c_0)$. The multiplier V enters just as before. Apart, then, from the multiplier $(3\eta V)^{-1}$ which affects all the integrals, the combined first terms of the first two integrals amount to

$$-\frac{3RT\mu}{4M} V (c_{j\sigma} - c_0) + \frac{RT}{2M} V \left[(c_{j\sigma} - c_0) - (c'_{j\sigma} - c_0) \right]$$

$$= \frac{RT}{2M} V \left\{ 1 - \frac{3}{2} \mu \left(1 + \frac{h\,\delta_{j\sigma}}{D_e} \right) \right\} \left(1 + \frac{h\,\delta_{j\sigma}}{D_e} + \frac{h\,\alpha_{j\sigma} r_j}{D_i} \right)^{-1} c ,$$

and the complete expression is obtained by summing as to σ, and subtracting half the sum of the corresponding expressions obtained when the subscript j is replaced by k and by l.

The third integral expresses the effect of the surface tension. Here a difficulty arises, for if we regard the cell as a parallelepiped the pressure due to the surface tension will be zero along the sides and infinite along the edges. Actually the curvature will be approximately that of an ellipsoid and we take

$$\gamma (r_k^{-1} + r_l^{-1})$$

as the approximate pressure on either face S_j, so that the force is

$$4\gamma (r_l + r_k),$$

and the corresponding term of the integral for the two opposite faces is

$$-8\gamma r_j (r_l + r_k) = -V\gamma (r_k^{-1} + r_l^{-1}).$$

This entire integral is therefore

$$V\gamma (r_j^{-1} - \tfrac{1}{2} r_k^{-1} - \tfrac{1}{2} r_l^{-1}).$$

To combine these results, we have now found for the approximate deformation equations the following form:

$$r_j^{-1}\frac{dr_j}{dt}=\frac{RT}{6\,\eta\,M}\sum_{\sigma}\left[1-\frac{3}{2}\mu\left(1+\frac{h\,\delta_{j\sigma}}{D_e}\right)\right]\left[1+\frac{h\,\delta_{j\sigma}}{D_e}+\frac{h\,\alpha_{j\sigma}\,r_j}{D_i}\right]^{-1}c+\frac{r}{3\,\eta}r_j^{-1}-\tfrac{1}{2}\{\cdots\}, \tag{6}$$

where the round brackets $\{\cdots\}$ denote the sum of the two expressions which are obtainable from the one written by changing the subscript j to k and to l in turn. These equations are derived from Betti's formula for plastic flow, and this, in turn, presupposes constant volume. We note, indeed, that the sum of the right members of the three equations (6) vanishes identically:

$$\sum r_j^{-1}\,dr_j=0\,,$$

which is equivalent to the statement

$$r_1\,r_2\,r_3=\text{const.}$$

3. *Equilibrium states.* If we denote by θ_j^{-1} the quantity exhibited on the right in (6), then these three equations have the form

$$r_j^{-1}\frac{dr_j}{dt}=\theta_j^{-1}-\tfrac{1}{2}(\theta_k^{-1}+\theta_l^{-1})\,. \tag{7}$$

These quantities θ_j have the dimension of time. Equilibrium occurs when the right members of (7) vanish, and this occurs only when the θ's are all equal:

$$\theta_1=\theta_2=\theta_3=\theta\,, \tag{8}$$

say. In fact, if the δ's and the α's are regarded as constant (e.g. the α's equal to $\frac{1}{2}$ and the δ's to half the cube root of the volume), we see that

$$\theta_j=\theta(r_j;\alpha_{j1}\,,\alpha_{j2}\,,\delta_{j1}\,,\delta_{j2})\,. \tag{9}$$

That is, regarded as functions of the variable r and the four parameters, the functions θ have the same functional form. In principle, equilibrium may be determined as follows. Solve

$$\theta(r;\alpha_1\,,\alpha_2\,,\delta_1\,,\delta_2)=\theta \tag{10}$$

for

$$r=R(\theta;\alpha_1\,,\alpha_2\,,\delta_1\,,\delta_2)\,, \tag{11}$$

set $\alpha_1=\alpha_{j1}\,,\cdots,\delta_2=\delta_{j2}$ to get

$$r_j = R_j(\theta), \tag{12}$$

solve

$$8R_1(\theta)\, R_2(\theta)\, R_3(\theta) = V \tag{13}$$

for θ, and finally insert this value of θ into (12).

In this procedure the concentration c enters as one of the parameters and we have thus obtained the r's as functions of c. If the variation of c is regarded as negligible this completes the determination of the equilibria. However, with variable c, we have obtained only the equilibrium values of the r's as functions of c. To complete the determination one must substitute these functions of c into the right member of (5), equate this to zero, solve for c, and employ this value for the numerical calculation of the equilibrium r's.

Unfortunately we cannot expect, in general, to obtain the equilibria in closed form since the equations (9) are quadratic in the r's, the functions R thus involve radicals, and when (13) is rationalized we may expect an algebraic equation of rather high degree. We are forced, therefore, to consider solutions and approximations in special cases.

4. *Types of equilibria in a uniform field.* When the external diffusion field is uniform and the cell is non-polar, we may at least drop the second subscripts on the δ's and the α's. Rashevsky, in fact, identifies all the δ's, and also all the α's, and we shall do likewise. If, more generally, the differences of the δ's, and those of the α's, are to be regarded as vanishing only with the differences of the r's, second and higher approximations can be obtained from the present considerations by introducing and solving for small deviations.

Rashevsky regards the δ's as equal to the smallest r. It simplifies the discussion considerably if we regard the δ's as equal to half the cube root of the volume of the cell, and this we shall do. Then dropping subscripts, the form of θ is given by

$$\theta^{-1} = A^{-1}[x^{-1} - \beta^2(1+x)^{-1}], \tag{14}$$

where

$$x = \frac{h\alpha r}{D_i(1 + h\rho/D_e)}, \quad A^{-1} = \frac{\gamma h\alpha}{3\eta D_i(1 + h\rho/D_e)}, \quad 8\rho^3 = V,$$
$$\beta^2 = \frac{RTD_i}{M\gamma h\alpha}\left[\frac{3}{2}\mu(1 + h\rho/D_e) - 1\right]c. \tag{15}$$

The quantity represented by β^2 could be positive or negative, and for the moment we may disregard the positiveness implied by the exponent.

If we let

$$\tau = \theta/A, \quad \sigma = \frac{h\alpha\rho}{D_i(1 + h\rho/D_e)}, \tag{16}$$

then the equilibria, for a given c, are given by the solutions x_j and τ of the four equations

$$\begin{aligned} \tau^{-1} &= x_j^{-1} - \beta^2(1 + x_j)^{-1}, \\ x_1x_2x_3 &= \sigma^3. \end{aligned} \tag{17}$$

An obvious solution is the equilibrium of spherical type

$$x_1 = x_2 = x_3 = \sigma, \tag{18}$$

and we shall later consider the stability of this equilibrium. For the present we wish to inquire as to the existence and character of equilibria of other types.

Non-spherical equilibria are given by solutions of (17) in which at least two of the x's are different. If $x_1 \neq x_2$, then

$$x_1^{-1} - \beta^2(1 + x_1)^{-1} = x_2^{-1} - \beta^2(1 + x_2)^{-1}$$

or, after suppressing the factor $x_1 - x_2$:

$$\beta^2x_1x_2 = (x_1 + 1)(x_2 + 1). \tag{19}$$

Similarly, if $x_3 \neq x_2$,

$$\beta^2x_3x_2 = (x_3 + 1)(x_2 + 1).$$

But these two equations imply that

$$x_1 = x_3,$$

whence *no equilibrium is possible for a non-polar cell in a uniform field with the three dimensions all unequal.*

For the non-spherical equilibria, therefore, we have to solve equations (19) and

$$x_1^2x_2 = \sigma^3 \tag{20}$$

for x_1 and x_2. Now the graph of (19) is a rectangular hyperbola which intercepts the axes at $(-1, 0)$ and at $(0, -1)$, and for which the line $x_1 = x_2$ is always an axis of symmetry. Since (19) may also be written

$$\left(x_1 - \frac{1}{\beta^2 - 1}\right)\left(x_2 - \frac{1}{\beta^2 - 1}\right) = \frac{\beta^2}{(\beta^2 - 1)^2}, \tag{21}$$

we see that the center lies at $[(\beta^2 - 1)^{-1}, (\beta^2 - 1)^{-1}]$. If $\beta^2 < 0$ the hyperbola does not intersect this fixed axis of symmetry at all, so that neither branch of the hyperbola enters the first quadrant and no intersections with (20) occur. Thus the equilibrium of spherical type is the only one possible. We therefore consider only the case of $\beta^2 > 0$.

If $\beta^2 < 1$ the hyperbola intersects the fixed axis of symmetry at $x_1 = x_2 = (\pm\beta - 1)^{-1}$ in the third quadrant. Hence again the hyperbola does not enter the first quadrant and only the spherical equilibrium is possible.

If $\beta^2 > 1$ one branch is entirely in the first quadrant. It is geometrically evident that these curves have two intersections (possibly coincident) or else none, and that for a given σ there are always two intersections if β is sufficiently large. *If*

$$\sigma > (\beta - 1)^{-1} \tag{22}$$

the curve (20) intersects the axis of symmetry of (19) inside the hyperbola and hence *the two non-spherical equilibria exist and one is of prolate type and one of oblate type. If* (22) *fails, there are either no intersections, or else there are two, both corresponding to equilibria of the prolate type.* Two equilibria of the oblate type cannot exist. This conclusion is at variance with a result previously obtained (Householder, 1941) where, by extending Rashevsky's calculations based upon the assumption of a spheroidal cell, conditions were found under which two equilibria of oblate type could exist. There δ was taken as equal to r_1, which presumably accounts for the discrepancy.

The relation (22) failing, there is a minimal value of β, for a given σ, for which the curves (19) and (20) intersect. This can be obtained by eliminating x_2 between the two equations and equating to zero the discriminant of the resulting equation. This yields a relation between β and σ. Since both quantities involve the volume, the expressions for β and σ in terms of the volume can be substituted in this and we obtain thus an equation giving the minimal volume of a cell which is capable of having non-spherical equilibria, the internal concentration being supposed fixed. The result of this calculation is omitted.

Relation (22) may be written in the form

$$\beta^2 > (\sigma + 1)^2/\sigma^2, \tag{23}$$

and if, in this, we insert for β^2 and σ their expressions in terms of ρ we obtain, when fractions are cleared and all terms transposed to the left, a cubic inequality in ρ. In this the leading coefficient is positive and the last two negative. Thus there is a minimal volume for which there exist non-spherical equilibria of opposite types.

We have so far neglected the variation of c. When this is considered, the equilibrium is determined by equating to zero the right member of (5), an equation which may be written

$$Q = \beta^2 \sum x_j^{-1}(1 + x_j)^{-1}, \tag{24}$$

$$Q = q/B, \quad B = \frac{h^3 \alpha^2 M \gamma}{RTD_i^2(1 + h\rho/D_e)^2[\frac{3}{2}\mu(1 + h\rho/D_e) - 1]}. \tag{25}$$

We need consider only the case $\beta^2 > 0$, and when this holds we have $B > 0$. Equation (24) together with (19), (20), and $x_1 = x_3$ give the required non-spherical equilibria, with β^2, which is proportional to c, regarded as one of the unknowns. We eliminate β^2 from (24) by means of (19) and obtain

$$\frac{x_1 + 1}{x_1 x_2^2} + \frac{2(x_2 + 1)}{x_1^2 x_2} = Q,$$

which, in view of (20), is equivalent to

$$x_1(x_1 + 1) + 2x_2(x_2 + 1) = Q\,\sigma^3\,x_2. \tag{26}$$

This is an ellipse whose eccentricity is $1/\sqrt{2}$, whose major axis is horizontal, and which intercepts the x_1-axis at the origin and at $x_1 = -1$. For Q (and hence q) sufficiently large the ellipse enters the first quadrant, and given any ρ a q may be determined sufficiently large so that (26) and (20) have two real intersections in this quadrant. The intersections exist and correspond to equilibria of opposite type (one oblate and one prolate) whenever

$$Q\,\sigma^3 > 3(\sigma + 1). \tag{27}$$

In case (27) fails, there is a narrow range of values of Q for which two non-spherical equilibria of the prolate type exist, while for all values of Q below this range the only equilibrium is the spherical one.

5. *Stability of the spherical equilibrium.* Let

$$x_j = \sigma(1 + \xi_j). \tag{28}$$

Equations (7) have then the form

$$\begin{aligned} A(1 + \xi_j)^{-1}\frac{d\xi_j}{dt} = \frac{1}{\sigma}\left\{(1 + \xi_j)^{-1} - \tfrac{1}{2}(1 + \xi_k)^{-1} - \tfrac{1}{2}(1 + \xi_l)^{-1}\right\} \\ - \frac{\beta^2}{1 + \sigma}\left\{(1 + \frac{\sigma}{1 + \sigma}\xi_j)^{-1} - \tfrac{1}{2}(1 + \frac{\sigma}{1 + \sigma}\xi_k)^{-1}\right. \\ \left. - \tfrac{1}{2}(1 + \frac{\sigma}{1 + \sigma}\xi_l)^{-1}\right\}. \end{aligned} \tag{29}$$

If we expand in power series and observe that

$$0 = \xi_1 + \xi_2 + \xi_3 + \cdots, \tag{30}$$

we have

$$\frac{d\xi_j}{dt} = \frac{\beta^2\sigma^2 - (1+\sigma)^2}{A\,\sigma(1+\sigma)^2} \cdot \frac{3}{2}\xi_j + \cdots \tag{31}$$

where terms of degree higher than the first have been omitted. For a fixed value of c, therefore, the equilibrium is stable provided

$$\beta^2\sigma^2 < (1+\sigma)^2, \tag{32}$$

that is, provided either β^2 is negative, or else β^2 is positive and (22) fails. Otherwise the spherical equilibrium is unstable. Hence *when non-spherical equilibria of opposite types (one prolate and one oblate) exist, the spherical equilibrium becomes unstable, but in all other cases the spherical equilibrium is stable and the approach to this equilibrium is monotonic.*

To include the variation in the concentration, we have to adjoin equation (5), which can be written

$$\frac{dc}{dt} = B\{Q - \beta^2 \sum x_j^{-1}(1+x_j)^{-1}\}. \tag{33}$$

Since β^2 is proportional to c:

$$\beta^2 = \Gamma c,$$

say, the equilibrium value of c is

$$c = c_0 \equiv \frac{Q\,\sigma(1+\sigma)}{3\,\Gamma}, \tag{34}$$

and if we set

$$c = c_0(1+\xi), \tag{35}$$

and expand, we have

$$\frac{d\xi}{dt} = -\frac{3AB}{\sigma(1+\sigma)}\xi + \cdots. \tag{36}$$

If we compare (25) and (15) and recall that A represents the coefficient of c in (15), we note that the product AB is always positive. The four linearized equations to be considered are now the three equations (31) in which β^2 is evaluated with $c = c_0$, and equation (36). Evidently the stability of the equilibrium is governed only by the signs in (31), since that in (36) is always negative, so that the conclusions with regard to stability remain as given.

This work has been aided in part by a grant from the Dr. Wallace C. and Clara A. Abbott Memorial Fund of the University of Chicago.

LITERATURE

Householder, A. S. 1941. "Mathematical Biophysics of Cellular Forms and Movements." *Bull. Math. Biophysics*, **3**, 27-38.

Rashevsky, N. 1940. *Advances and Applications of Mathematical Biology.* Chicago: University of Chicago Press.

Williamson, Robert R. "Growth, Organization and Differentiation in Cellular Aggregates." To be published.

BULLETIN OF
MATHEMATICAL BIOPHYSICS
VOLUME 4, 1942

THE LINEAR THEORY OF NEURON NETWORKS: THE STATIC PROBLEM

WALTER PITTS
THE UNIVERSITY OF CHICAGO

The construction of a theory of activity in neuron networks of arbitrary topological structure is commenced under the linear excitation hypothesis: we consider conditions for possible steady-state equilibria, deferring a dynamical treatment to the sequel.

I. Introduction and Preliminary Definitions.

In four previous papers published in this Bulletin (1941a, b, c, 1942; to be hereinafter referred to as I, II, III, IV respectively) A. S. Householder has considered the nature of steady-state activity in nerve-fiber networks under constant stimulation, and has derived detailed results for several specific types of networks. The following observations will treat this same problem, and will presuppose for their understanding a reading of the papers mentioned. Our purpose in particular will be to develop a somewhat different approach to the question; we shall show how this alternative procedure enables us both to calculate explicitly all the patterns of steady-state activity which are consistent with the applied stimulation in the most general possible network—albeit by a rather laborious procedure—and to lay the groundwork for a theory of transient excitation.

We shall make an assumption with regard to the activity of a fiber as a function of stimulation which is slightly more general than the simple linearity of I, II, III, and IV: we shall suppose that, as the stimulation increases, the fiber remains inactive until the threshold is reached, then for some range it is a linear function of the excess of the stimulation over the threshold; and finally when the stimulation reaches a certain upper limit, the resulting excitation has a constant value for this and all greater stimulations. This hypothesis seems in better agreement with the customary suppositions than that of simple linear increase above the threshold, while it occasions us no further theoretical difficulties. In particular, the reader will perceive the perdurable validity of lemma 1 of Pitts 1942 (hereinafter referred to as V) which, indeed, requires little more than that the excitation function should be continuous and monotone.

In a given network $\mathcal{N}$, which it is convenient to suppose is not a simple circuit, we may usefully classify the synapses into three groups. The *first-order* synapses will be those which join links in a simple chain, having just one afferent and one efferent fiber; the *second-order* synapses are simple branch-points, with one afferent and several efferent fibers; and the *third-order* synapses, representing convergence-points, possess several afferent and one or more efferent fibers. We may simplify $\mathcal{N}$, without changing its activity properties essentially, by removing all the second-order synapses; this may be accomplished in the following way. If s_i be such a synapse, say with n efferent fibers $d_1, d_2, \cdots d_n$, follow the afferent chain to s_i contrary to its sense until the next preceding second or third-order synapse, say s_j, is reached. Construct n simple chains of fibers such that, for any p, the p-th fiber in any of them has the same threshold and activity parameter as the p-th fiber on the chain between s_j and s_i. Strike out s_i and the chain from s_j to s_i, and connect instead the afferent end of all the constructed chains to s_j, and each one of the n efferent ends to one of the n fibers which formerly began at s_i. Repeat this process until no second-order synapses remain. The result will be a network $\mathcal{N}'$ which consists of say P third-order synapses, interconnected by some Q simple chains. These synapses may be enumerated as s_1, $s_2, \cdots, s_P$, and the chains as $c_1, c_2, \cdots, c_Q$. Henceforth, we shall use the term ‘synapse’ to mean ‘third-order synapse’, when not otherwise specified.

The topological structure of $\mathcal{N}'$, regarded as a complex of chains and synapses, may be represented by two functions of integers in the following way. $\phi(i, j) = \phi_{ij}$ is defined to be unity if the chain c_i leads to the synapse s_j; otherwise it is zero. $\psi(i, j) = \psi_{ij}$ is unity if the chain c_i leads *from* the synapse s_j, and otherwise zero. The reader will have remarked that if we consider the chains c_i as 1-complexes and the synapses s_j as 0-cells in a linear graph, the orientation matrix Ξ of $\mathcal{N}'$ is $||\phi_{ij}|| - ||\psi_{ij}||$; while conversely, given a Ξ, we may obtain $||\phi_{ij}||$ and hence ϕ by replacing all negative entries with zero; and $||\psi_{ij}||$ by nullifying positive entries and multiplying by -1.

Various metrical characteristics of the chains c_i will be important. Among these are the number of fibers in c_i, to be denoted by ‘ν_i’; the product of the activity parameters of fibers of c_i, to be designated by ‘A_i’; and the quantities μ_i, defined thus: let σ be the external stimulation at the s-th synapse of c_i (counting its origin as the first), less the threshold of the succeeding fibers, and $p_1, p_2, \cdots, p_{\nu_i}$ the activity parameters of the fibers of c_i, in order: μ_i is then

$$p_{\nu_i}\sigma_{i,\nu_i} + p_{\nu_i}\, p_{\nu_{i-1}}\, \sigma_{i,\nu_{i-1}} + \cdots + A_i\, \sigma_{i,1}.$$

The μ_i correspond to the quantities $\sigma_i{}^{(n)}$ used for the simple circuit in I, II, III, and IV. Next, we shall require the quantities y_i, which will be employed in a slightly different usage than in I, II, III, and IV: y_i will be the total activity at the synapse s_i, diminished by the value of σ_i for this synapse. Further, given a chain c_i leading from s_j to s_k, we shall define Λ_i as the greatest lower bound of the values of y_j which set c_i into complete activity with the given pattern of external stimulation at the synapses within c_i, and Υ_i as the least upper bound of such values. With respect to each chain c_i, moreover, and the synapse s_j whence it leads we may specify a pair of quantities, α_i, β_i, to be called the *multipliers* belonging to that chain. We shall set $\alpha_i = 1$ if $y_j \geqq \Lambda_i$; otherwise $\alpha_i = 0$. If $y_j > \Upsilon_i$, $\beta_i = 0$; otherwise $\beta_i = 1$. Clearly, its multipliers characterize the state of c_i completely: in particular, c_i is in complete activity if and only if $\alpha_i \beta_i = 1$.

We may observe first that the state of a network $\mathcal{N}$ over a period of time is determined completely by the value of the y_i at its third-order synapses during that interval; this follows, by a remark made in I, from the circumstance that all other synapses are connected to a third-order synapse by a simple chain. If, then, we regard the values of these y_i as components of a point-vector $\bar{y}$ in a suitable P-space, the motion of that point is precisely correlated to changes in the state of the network. This representation will be found decidedly useful; we may extend it as follows. Along any coordinate axis y_i corresponding to the excitation at s_i, we erect perpendicular hyper-planes corresponding to the values $\Lambda_j, \Lambda_k, \Lambda_l, \cdots, \Lambda_m; \Upsilon_j, \Upsilon_k, \cdots, \Upsilon_m$ of y_i, where $c_j, c_k, \cdots, c_m$ are the chains leading from s_i. The totality of such planes will divide the whole P-space into boxes or compartments, each of which will be called a *region.* Each region Γ_ρ corresponds to a single activity pattern for the chains of $\mathcal{N}$; we shall see that the path of the point $\bar{y}$, as it moves concomitantly with variation in the state of $\mathcal{N}$, has no corners within a region, and only, if at all, on the boundaries.

Thus to every region Γ_ρ there is assigned a unique distribution of the values zero and one for the multipliers of chains of $\mathcal{N}$, which holds for $\mathcal{N}$ whenever $\bar{y}$ is in Γ_ρ; and conversely, for every set of values for the multipliers which makes no pair of them concomitantly zero, we may correlate a unique region. Given Γ_ρ, we shall specify its multiplier-distribution by the pair of sets $\pi_{\rho_1}, \pi_{\rho_2}$, where π_{ρ_1} contains all multipliers which vanish in Γ_ρ, and π_{ρ_2} those which are unity there.

We may call a point $\bar{x}$ of P-space an *equilibrium point* of $\mathcal{N}$ if there exist a steady state of $\mathcal{N}$ determined by $\bar{y} = \bar{x}$ and consistent with the given external stimulation. A region is *stable* if it contain an equilibrium point; otherwise *unstable*. It will be seen that the steady-state problem treated for various cases in I, II, III and IV is essentially a problem in statics, i.e., that of determining all the stable regions for a given network having a given applied stimulus pattern. This we shall call the *static problem*; and we shall now proceed to find an explicit solution thereof for the general network $\mathcal{N}$.

II. The Static Network Problem.

Consider the stimulation at a synapse s_i in the steady state. It will, in general, be the sum of several types of contribution. First, of course, we have the external stimulation σ_i applied at s_i. Second, there is the contribution of the chains leading to s_i: this may be computed as follows. Certain of these chains, say $c_{i_1}, c_{i_2}, \cdots ; c_{i_H}$, will be in complete activity and will consequently deliver an excitation $A_{i_a} y_{[i_a]} + \mu_{i_a}$, where $s_{[i_a]}$ is the synapse where c_{i_a} commences. Another group of chains, say $c_{i_{H+1}}, \cdots , c_{i_K}$, which are not in complete activity; will deliver generally an excitation $A_{i_b} \Lambda_{i_b} + \mu_{i_b}$; and the remainder, $c_{i_{K+1}}, \cdots , c_{i_L}$, will contribute an amount $A_{i_c} \Upsilon_{i_c} + \mu_{i_c}$. Adding these, we obtain

$$y_i = \sum_{j=1}^{L} \mu_{i_j} + \sum_{j=1}^{H} A_{i_j} y_{[i_j]} + \sum_{j=H+1}^{K} A_{i_j} \Lambda_{i_j} + \sum_{j=K+1}^{L} A_{i_j} \Upsilon_{i_j} . \tag{1}$$

If we recall some of the quantities defined earlier, we shall be able to write (1) more compendiously as

$$\begin{aligned} y_i = \sum_j \{ \phi_{ji} \mu_j + \sum_k \psi_{jk} \; \phi_{ji} \alpha_j \beta_j A_j y_k + A_j \phi_{ji} [\Lambda_j (1 - \alpha_j) \\ + \Upsilon_j (1 - \beta_j)] \}, \end{aligned} \tag{2}$$

where the summations are now taken over all chains and all synapses. The apparent extra terms which are in (2) but not in (1) vanish through a zero value for some of the multipliers, the ϕ_{ij}, or the ψ_{jk}.

An equation of the kind (2) may be written for every synapse: if we put

$$\begin{aligned} M &= || \sum_j \phi_{ji} \psi_{jk} \alpha_j \beta_j A_j || , \\ R &= || \sum_i \phi_{jk} (\mu_j + A_j [\Lambda_j (1 - \alpha_j) + \Upsilon_j (1 - \beta_j)]) || , \end{aligned} \tag{3}$$

we may write the system in matrix form as

$$(I - M)\bar{y} = R\,. \tag{4}$$

We shall suppose for the moment that the matrix $I - M$ is non-singular, and return presently to cases where this does not hold. Under this hypothesis, the system (4) may be solved formally for the y_i, treating the unknown α's and β's as indeterminates, by Cramér's rule: this yields a set of expressions for the y_i which are the quotients of polynomials in the multipliers with known coefficients by the determinant $|I - M|$:

$$y_i = \frac{1}{|I - M|} \sum_j R_j [I - M]_{ij}\,, \tag{5}$$

where $[I - M]_{ij}$ is the co-factor of the element i,j in $I - M$.

Now it is clear that any given distribution π_{ρ_1}, π_{ρ_2} of the multipliers will determine a stable region if and only if the values for the y_i resulting by substitution of the given α's and β's in (5) satisfy the inequalities involved in the definitions of the multipliers. In particular, if c_l emanate from s_i, then the inequalities

$$y_i = \frac{1}{|I - M|} \sum_j R_j [I - M]_{ij} \overset{\geq}{=} \Lambda_l \tag{6}$$

must hold respectively as $\alpha_l \;\varepsilon\; \pi_{\rho_2}$ or $\alpha_l \;\varepsilon\; \pi_{\rho_1}$, with a similar set for the β's. These requirements may be expressed conjointly by

$$\begin{aligned} (2\,\alpha_l - 1)\,y_i &> (2\,\alpha_l - 1)\,\Lambda_l \\ (1 - 2\,\beta_l)\,y_i &> (1 - 2\beta_l)\,Y_l \end{aligned} \tag{7}$$

for all such j and l, which is

$$\begin{aligned} &\frac{\sum\limits_{j,k} \psi_{ij}\,(2\,\alpha_i - 1)\,R_k |I - M|_{jk}}{|I - M|} - \sum_j\,(2\,\alpha_i - 1)\,\psi_{ij}\,\Lambda_i > 0 \\ &\frac{\sum\limits_{j,k} \psi_{ij}\,(1 - 2\,\beta_i)\,R_k |I - M|_{jk}}{|I - M|} - \sum_j\,(1 - 2\,\beta_i)\,\psi_{ij}\,Y_i > 0: \end{aligned} \tag{8}$$

The requirements (8) thus form necessary and sufficient conditions that a set of α's and β's should determine an equilibrium point. They may be replaced by a set which is multilinear in the multipliers, by making successively the assumptions that $|I - M|$ is positive and that it is negative, multiplying by this determinant in (8), and adding the corresponding supposition to the set of multilinear inequalities so generated. Higher powers of the α's and β's need not occur in these, since they may always be reduced to linear occurrences by remembering $\alpha_i^2 = \alpha_i$, $\beta_i^2 = \beta_i$. The resulting conditions will then have the form

$$\sum_{I_j, K_l} P^{(m)}_{I_j, K_l} \alpha_{I_1} \alpha_{I_2} \cdots \alpha_{I_j} \cdots \beta_{K_1} \beta_{K_2} \cdots \beta_{K_l} + H_m > 0. \tag{9}$$

Since the number of multipliers altogether is finite, and each of them assumes only the two possible values 0 and 1, the set (9) may always be solved in any particular case by substituting in (9) all the possible value distributions, and rejecting all which do not fit. There are 3^Q such distributions altogether, Q being the number of chains, so that the labor might be supposed very great; but in practice the vast majority of possible distributions may be found to satisfy or fail to satisfy (9) by inspection. In any case, the problem is one primarily of computation; the explicit solutions are not required to deduce the general properties of neuron networks, and consequently, while undoubtedly desirable, an expeditious numerical method is not to be regarded as an essential part of the problem; the more so in that discussions such as our own have as their principal object the enunciation of general propositions as to types of possible activity, rather than practical application to specific networks. We may remark, incidentally, that of the distributions π_{ρ_1}, π_{ρ_2} which satisfy (11), those which require both members of some pair α_j, β_j to vanish may be discarded immediately, as corresponding to no region Γ_ρ. This is the source of the number 3^Q given above for the number of possible distributions.

We may return now to the case where $|I - M|$ vanishes, either identically or for certain particular multiplier-distributions. Given such a distribution π_{ρ_1}, π_{ρ_2}, we may distinguish two cases. In the first, the matrix produced by adding R as an additional column to $I - M$, (into which we have substituted the values assigned by π_{ρ_1}, π_{ρ_2} to the multipliers) has a greater rank than $I - M$ itself. In this case the equations (4) are inconsistent, no vector $\bar{x}$ of Γ_ρ satisfies them, and there is accordingly no equilibrium point in Γ_ρ. The second case, where the augmented matrix has the same rank as $I - M$ itself, is more interesting. If q be the nullity of $I - M$, q of the variables y_i may be chosen arbitrarily, and the equations (4) will then suffice to determine values for the remaining coordinates such that the constellation fixes an equilibrium-point. In this case, therefore, instead of having a single equilibrium point in the region, we have a q-dimensional locus of them, so that even knowledge of both the activity pattern and the applied stimulation does not enable us to find the steady-state excitation in a unique way. We shall see later, in considering the dynamical network-problem, that under these circumstances the asymptotic behavior of the system is determined essentially by the initial position of the network-vector.

This work was aided in part by a grant from the Dr. Wallace C. and Clara A. Abbott Memorial Fund of the University of Chicago.

LITERATURE

Householder, A. S. 1941a. "A Theory of Steady-State Activity in Nerve-Fiber Networks: I. Definitions and Preliminary Lemmas." *Bull. Math. Biophysics*, **3**, 63-70.

Householder, A. S. 1941b. "A Theory of Steady-State Activity in Nerve-Fiber Networks: II. The Simple Circuit." *Bull. Math. Biophysics*, **3**, 105-112.

Householder, A. S. 1941c. "A Theory of Steady-State Activity in Nerve-Fiber Networks: III. The Simple Circuit in Complete Activity." *Bull. Math. Biophysics*, **3**, 137-140.

Householder, A. S. 1942. "A Theory of Steady-State Activity in Nerve-Fiber Networks: IV. N p Circuits with a Common Synapse." *Bull. Math. Biophysics*, **4**, 7-14.

Pitts, Walter. 1942. "Some Observations on the Simple Neuron Circuit." *Bull. Math. Biophysics*, **4** , 121-129.

BULLETIN OF
MATHEMATICAL BIOPHYSICS
VOLUME 4, 1942

SOME PROBLEMS IN MATHEMATICAL BIOPHYSICS OF VISUAL PERCEPTION AND AESTHETICS

N. Rashevsky
The University of Chicago

The paper outlines a further extension of a previous theory. It discusses perception of straight lines, perception of length, perception of intersections, disconnected contours; effects of associations; breaking up of a pattern into parts; some suggestions for experimental procedure.

In previous publications (Rashevsky 1938, 1940) we have outlined a biophysical theory of visual perception, which among other things, led to a physicomathematical theory of aesthetic values of simple geometric pattern. The comparison of theoretically calculated aesthetic values for 10 simple polygons with experimentally determined rank order values for the same patterns gave a rather good agreement. Our next step therefore should be to improve and generalize the theory, so as to be able to apply it to more complex cases. The purpose of the present paper is to outline the way for such a generalization. To avoid repetitions we presuppose familiarity of the reader with the above two references.

1. *Perception of straight lines.* In *loc. cit.* we assumed as a very rough approximation, that the distinct groups of neurons, corresponding to different vertical components of the eye-movements have all the same excitation (Rashevsky, 1938, p. 285; 1940, p. 188). That such a simple situation cannot hold exactly, follows from the general discussion of neural mechanism involved. To each intensity stimulus there corresponds a group of neurons lying in different threshold intervals h_1, h_2. In a series of important papers, A. S. Householder (1939, 1940 a, b) has applied this concept to the theory of intensity discrimination, which leads to a rather good representation of experimental data. We may apply his results directly to our problem.

Using the same notations as Householder (1939; also Rashevsky, 1940, chap. x), we have for the determination of h_1 and h_2 the equation:

$$\Phi(S_1 h_1) = \Phi(S_1 h_2) = \frac{\lambda \int_{h_1}^{h_2} \Phi(S_1 h)\, dh}{1 + \lambda(h_2 - h_1)}. \qquad (1)$$

The total intensity of excitation of all neurons with thresholds between h_1 and h_2 is nothing else but the quantity $I(S)$ of Householder, and is given by

$$I(S) = \frac{\lambda \int_{h_1}^{h_2} \Phi(S, h)\, dh}{1 + \lambda(h_2 - h_1)}. \tag{2}$$

If v is the hypothetical constant velocity of scanning (*loc. cit.*), then for the excitation of the V center, the quantity S is given by

$$S = S_v = av \cos\theta\,, \tag{3}$$

where a is a coefficient of proportionality. For a given Φ, which itself is determined by the distribution function $f(h)$ of the thresholds of the central neurons, the total intensity of excitation of a V center is for every value of the angle θ given by equations (2) and (3).

For an H center, S is given by

$$S = S_H = bv \sin\theta\,, \tag{4}$$

where b is another coefficient of proportionality. Equations (2) and (4) determine now the intensity of excitation of the H center for any value of θ.

Assuming different values for the coefficients a and b in equations (3) and (4), we ascribe different weights to the vertical and horizontal components. In this way we should be able to take into account the possible preference for the vertical direction, noticed in *loc. cit.* The values of a and b will enter as parameters into the final expression for the aesthetic measure of a pattern any may be determined by comparison of the theory with experiment. The final aim of the theory should be to calculate a and b theoretically from assumptions about the peripheral neural mechanism.

As regards the shape of the function $\Phi(S, h)$, we may try, with Householder (1939), the simplest assumption, putting:

$$\Phi(S, h) = h(S - h). \tag{5}$$

In view of the good agreement of this assumption with data on intensity discrimination, it will probably suffice as a first approximation. Eventually more complex assumptions about $\Phi(S, h)$ will have to be investigated.

2. *Perception of lengths.* A similar procedure may be used for the calculation of the intensity of excitation of the L center for any given length of a straight line. For a very rough approximation we may set here S proportional to the length of the straight line perceived. A recent study of Householder (1940 b) shows, however, the

necessity of a somewhat more complex mechanism, and his results may be taken over almost directly.

3. *Perception of angles.* If the fibers leading to the V or H centers send off collaterals to other centers, A^*, these collaterals being mixed fibers, characterized by either (Rashevsky, 1940)

$$A > B; \quad a > b; \quad \frac{A}{a} < \frac{B}{b}; \tag{6}$$

or by

$$A < B; \quad a < b; \quad \frac{A}{a} > \frac{B}{b}; \tag{7}$$

then any sufficiently strong *sudden* increase of the vertical stimulus (3) or of the horizontal stimulus (4) will result in a brief excitation of A^*, through the collaterals satisfying relations (6). Similarly any sufficiently strong sudden decrease of those stimuli will result in an excitation of A^* through fibers satisfying relations (7). For sake of definiteness let us consider the case of a sudden increase of the vertical component. The other cases are treated in a similar way.

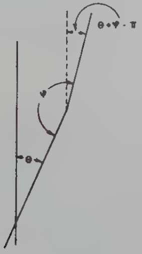

FIGURE 1

The stimulus consists now in the sudden increase of the vertical component, and is equal (Figure 1) to

$$\begin{aligned} S_{v+} &= a_1 a v [\cos(\theta + \phi - \pi) - \cos\theta] \\ &= - a_1 a v [\cos(\theta + \phi) + \cos\theta], \end{aligned} \tag{8}$$

where a_1 is again a coefficient of proportionality, different from a. Thus S_{v+} is a function both of the magnitude of the angle ϕ and of its position, as determined by θ.

The asymptotic values of ε and j at the efferent end of the collateral fiber of type (6), are, for constant θ, of the form:

$$\varepsilon_0 = \frac{AE}{a}; \qquad j_0 = \frac{BE}{b}; \tag{9}$$

where E is a linear function of S_v. The change S_{v+} results in an increase of E by an amount ΔE, ΔE being proportional to S_{v+}. Hence, denoting by a_2 the coefficient of proportionality, which can readily be expressed in terms of the different constants of all the fibers involved (Rashevsky, 1938 a, chap. xxii), we have

$$\Delta E = a_2 S_{v+} . \tag{10}$$

Because of (6), we have $\varepsilon_0 < j_0$.

The sudden increase ΔE at the time $t = 0$ results in a variation of ε and j according to

$$\begin{aligned} \varepsilon &= \frac{AE}{a} + \frac{A\Delta E}{a}(1 - e^{-at}) ; \\ j &= \frac{BE}{b} + \frac{B\Delta E}{b}(1 - e^{-bt}) . \end{aligned} \tag{11}$$

If ΔE is sufficiently large, then ε exceeds j at a time t_1, and then again drops below it at the time t_2. Those two moments are given by the roots of the transcendental equation, obtained by putting $\varepsilon = j$ and using equations (11). The threshold value of ΔE, which must be exceeded in order that ε shall temporarily exceed j is calculated in the same manner as the rheobase in the two-factor theory of peripheral excitation (Rashevsky, 1938 a).

A solution of the transcendental equation which determines t_1 and t_2 cannot be given in a closed form. An immediate practical problem therefore is to find a sufficiently good approximation for it. Such an approximation gives us t_1 and t_2 in terms of ΔE, and hence, because of equation (10), also in terms of S_{v+}. Thus

$$t_1 = t_1(S_{v+}) ; \qquad t_2 = t_2(S_{v+}) . \tag{12}$$

In *loc. cit.* we considered, that the temporary excess of $\varepsilon - j$ at the efferent end of the collateral acts as a stimulus upon the afferent end of another fiber, whose efferent end is connected to a similar mechanism as assumed in the theory of intensity discrimination. This will result in an excitation of a group of neurons in an "A − center", such that to each positive value of $\varepsilon - j$ at A^* (Figure 2) there will corre-

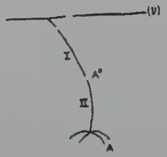

FIGURE 2

spond a distinct group of neurons at A. The relation between $\varepsilon - j$ at A^* and the total intensity of excitation of the corresponding group at A is of the same form, as the relation (2), in which $\varepsilon - j$ plays the role of S.

We must however remember, that $\varepsilon - j$ at A^* is not constant, but varies according to

$$\varepsilon - j = E\left(\frac{A}{a} - \frac{B}{b}\right) + \Delta E\left(\frac{A}{a} - \frac{B}{b} - \frac{A}{a}e^{-at} + \frac{B}{b}e^{-bt}\right). \qquad (13)$$

It is positive only between t_1 and t_2. It is effective even within narrower limits of t. If namely h denotes the threshold of fiber II (Figure 2), then $\varepsilon - j$ is effective only when it exceeds h. This happens between two time values t'_1 and $t'_2 > t'_1$, which are the roots of the equation in t, obtained by equating the right hand side of (13) to h. Hence in the expression (2) the intensity $I(S) = I(\varepsilon - j)$ will be also a function of time. This function $I(t)$ is obtained by substituting in equation (2) $\varepsilon - j$ for S, and then introducing equation (13) for $\varepsilon - j$. Since equation (13) depends on ΔE, and hence on S_{v+}, therefore S_{v+} will also enter as a parameter in the expression for $I(t)$, so that we may write $I(S_{v+}, t)$. The total excitation intensity of the A — center is given by

$$I(S_{v+})_{tot} = \int_{t'_1}^{t'_2} I(S_{v+}, t)\, dt. \qquad (14)$$

By means of equation (8) we may express $I(S_{v+})_{tot}$ in terms of φ and θ.

We may also consider an alternate assumption. We may consider the value

$$\int_{t'_1}^{t'_2} (\varepsilon - j)\, dt, \qquad (15)$$

which can be obtained from equation (13), as the total value of the stimulus S in equation (2). This will give us in general a different expression for $I(S_{v+})_{tot}$ in terms of φ and θ. The technical problem involved in both cases is the calculation of t_1, t_2, t'_1, and t'_2 in approximate closed form.

The case of a sudden increase of the horizontal component is treated in a similar way. For the sudden decrease of either the vertical or horizontal component we have a very similar problem, except that we now have a fiber satisfying relations (7).

We may consider that all collaterals either of type (6) or of type (7), innervated either by the vertical or horizontal component, converge to the same center A. The total excitation of such a center, corresponding to a given angle φ, is then obtained by summing the contributions due to S_{v+} (increase of vertical component), S_{v-} (decrease of vertical component); S_{H+} (increase of horizontal component) and S_{H-} (decrease of horizontal component).

As an alternative, we may consider however, that each of the above four cases corresponds to the excitation of four distinct A centers. The perception of an angle would thus always correspond to the excitation of four groups of neurons. Analytical expressions for the two different assumptions should be derived.

In *loc. cit.* we assumed that only the *upward* scanning of a line was effective. In that case, as easily seen, the perception of an angle situated as in Figure 3a will consist in complete interruptions of the vertical component $a \cos \theta_1$ together with the horizontal component $b \sin \theta_1$ ($S_{v-} = - a_1 a \cos \theta_1$; $S_{H-} = - a'_1 b \sin \theta_1$), *and* of the vertical component $a \cos \theta_2$ together with the horizontal component $b \sin \theta_2$ ($S_{v-} = - a_1 a \cos \theta_2$; $S_{H-} = - a'_1 b \sin \theta_2$). The total excitation in the A center will then depend *explicitly* only on θ_1 and θ_2, but not on φ. If on the other hand we have the case of Figure 3b, the perception of the upper end of the line corresponds only to $S_{v-} = - a_1 a \cos \theta_1$; $S_{H-} = a'_1 b \cos \theta_1$, which results in a different excitation in the A-center than before.

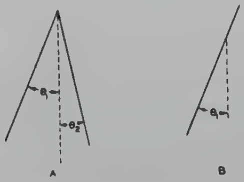

FIGURE 3

For the lower end on the other hand we have $S_{v+} = a_1 a \cos \theta_1$, $S_{H+} = a'_1 b \sin \theta_1$, which gives a still different excitation in the A center.

4. Perception of curves: As outlined in *loc cit.* the perception of a curve involves essentially the same neural mechanism as the perception of an angle. It is due also to changes in the vertical and horizontal components, with the difference however, that those changes are not sudden but gradual.

Consider the curve of Figure 4. According to the adopted mechanism (*loc. cit.*), its perception involves two separate upward scannings: ABC and ADC. Scanning of AB results in an increase of the vertical component from zero to av. This may cause an excitation at the efferent end of a collateral of type (6), the excitation being determined by the shape of the curve. If the equation of AB is given

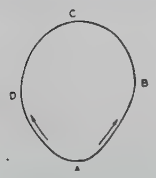

FIGURE 4

in cartesian coordinates as

$$y = f(x)\,; \tag{16}$$

then the distance along the curve of any point A' from A is equal to

$$s = \int_{x_A}^{x_{A'}} \sqrt{1 + \left(\frac{df}{dx}\right)^2}\, dx\,, \tag{17}$$

where x_A and $x_{A'}$ are the abscissas of the points A and A' correspondingly. Assuming as before, that the curve is scanned with constant velocity v, and putting $t = 0$ for the moment of fixation of the point A, we have:

$$s = vt\,. \tag{18}$$

Equation (16), (17) and (18) give us x and y for any point A' of the curve as functions of t:

$$x = x(t)\,; \qquad y = y(t)\,. \tag{19}$$

The vertical component stimulus S_v at any given point A' of the curve is given by

$$S_v = av \cos\theta = av \frac{df/dx}{\sqrt{1 + (df/dx)^2}}\,. \tag{20}$$

Because of (19), we can express S_v as a function of t:

$$S_v = S_v(t)\,. \tag{21}$$

We thus have a time variable S_v, and this will result in a variable excitation in the V center, $I[S_v(t)]$. The total excitation in the V center, corresponding to the scanning of AB, is given by

$$I_{tot} = \int_0^{t_B} I(S_v)\, dt\,, \tag{22}$$

where t_B is the time corresponding to the point B, and is given by

$$t_B = AB/v\,. \tag{23}$$

Besides the excitation of the V center, a variable S_v of the type considered will result also in an excitation of the A^* center through fibers of type (6). To obtain now the amount of excitation at A^*, we remember that at A^*

$$\frac{d\varepsilon}{dt}=AE-a\varepsilon; \qquad \frac{dj}{dt}=BE-b\varepsilon, \tag{24}$$

where E is a linear function of S_v, and is therefore a known function of t. Integrating equation (24) and setting $\varepsilon - j = 0$, we shall determine the moments t'_1 and t'_2 between which $\varepsilon - j > h$, and then proceed as in section 3; that is either consider

$$\int_{t'_1}^{t'_2} (\varepsilon - j)\, dt$$

as the total stimulus, to be used in equation (2) for S, or perform the integration over $I(S)$.

A general theory of this kind may be of relatively little use, just because of its generality. There are, however, definite specific problems that are of practical importance.

First we may consider AB as an arc of a circle. The differential equations (24) are in this case easily integrated, although the determination of t'_1 and t'_2 again requires approximate solutions of transcendental equations.

Next we may either study some simplest analytical curves, like parabola, cubic, etc. or try to derive some general theorems. One might investigate for instance whether a curve whose curvature decreases from A to B gives in general a stronger or a weaker excitation of the V and A centers, than a curve whose curvature increases from A to B.

A scanning of AB results also in a decrease of the horizontal component from bv to zero. In a similar way we may calculate the total excitation of the H center during the period of scanning, as well as the excitation in the A center, produced through collaterals of type (7).

Similarly scanning BC gives a decreasing S_v and an increasing S_H. The same considerations hold for ADC. We must keep in mind that for differently variable S_v and S_H we not only have different intensities of excitation in the V, H and A centers, but that in each case *different groups of neurons* are excited. If, as we have done in *loc. cit.*, we assume that approximately all those distinct groups have the same intensity of excitation, we obtain the following picture for the excitation pattern of a closed curve, such as shown on Figure 4. Denoting by S_{v+}, S_{v-}, S_{H+} and S_{H-} stimuli corresponding to *sudden* changes due to perception of angles, let us denote corresponding *gradual* changes by $\overline{S}_{v+}$, $\overline{S}_{v-}$, $\overline{S}_{H+}$, $\overline{S}_{H-}$. Then the scanning of the curve of Figure 4 results in 2 stimuli $\overline{S}_{v+}$, 2 of $\overline{S}_{v-}$, 2 of $\overline{S}_{H+}$ and 2 of $\overline{S}_{H-}$. This gives 4 groups of neurons in V; 4 groups in H; and 8 groups in A. Moreover we have 2 groups in the L-center, due to the perception of the 2 lengths ABC and ADC. Altogether there are 18 groups. Herefrom we may calculate the total excitation just as we have done in *loc. cit.* As is easily verified, if we change the shape of the curve, so as to introduce an inflection point (Figure 5), we obtain a different number of groups, since scanning from A to A' gives first an $\overline{S}_{v+}$, then $A'A''$ gives a $\overline{S}_{v-}$ and $A''B$ gives again a $\overline{S}_{v+}$. With the change of the number of neuronic groups the total excitation and therefore the aesthetic value of the figure will have changed.

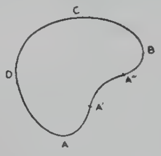

FIGURE 5

For a circle we must put, because of symmetry (*loc. cit.*), the two S_{v+} groups as identical, that is as one group with double intensity, and similarly for the two S_{v-} groups.

With these approximations we could calculate in the manner used in *loc. cit.* the aesthetic values of any combination of straight lines and curves. However it is very doubtful, whether the assumption of equal intensity of excitation of all groups represent even a rough approximation in case of complex patterns. It is therefore more advisable to elaborate the theory of perception of curves in the manner outlined in this section, before proceeding to comparisons with experiments.

5. Intersections. Disconnected contours. Consider the point O in Figure 6. We actually see four angles at this point. However it may be questioned whether the corresponding intensities I in the A center will be the same, as if the four angles were lying separately. Whereas in the perception of the angle E, there is no choice and no possibility of avoiding the angle, in scanning CEA, in the case of O

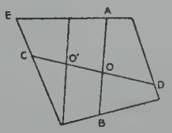

FIGURE 6

we may either scan *COD*, or *COA* or *COB* or *AOB*, etc. For each method of scanning we perceive only *one* angle or no angle at all. Therefore, in following such a pattern as in Figure 6, the relative frequency of the excitation corresponding to such an angle as *AOD* will be smaller than that corresponding to the angle *E* . Accordingly we shall attribute a lesser weight to the excitation of the center corresponding to *AOD* , by multiplying it by a true fraction, determined by the above probability considerations. This fraction is determined by the configuration at the intersection; it will for instance be less for *AOD* than for *ECO'*.

Similarly we perceive in Figure 6 not only the length *CD* , but also *CO'*, *O'O*, *OD*, *CO* and *O'D*. One should investigate whether these should be equally weighted. The answer to that question may also be found by considering in how many possible ways the whole geometric pattern may be scanned and how frequently a particular segment of a straight line will be scanned for each way. These questions do not arise for simple closed contours, such as discussed in *loc. cit.*

Another important problem concerns the neurological mechanism of the perception of several distinct, geometrically not connected patterns. Suppose we see two squares simultaneously. Since we argued in *loc. cit.* that parallel lines, as well as identical angles excite identical *V* , *H* and *A* centers, we may think that the total excitation from two squares is twice the excitation produced by one. This however is not necessarily so, and even appears unlikely. What happens is this: In scanning a simple closed contour rapidly, the average intensity of excitation of a given center is proportional to the relative frequency with which this center is excited per unit time. If we first scan one polygon then transfer our eye to another one and scan the latter, the number of times a given center becomes excited per unit time remains unchanged. An additional excitation is however provided by the movement of the eye from one polygon to another. This transfer movement may itself form a definite pattern. For instance we may have five circles, arranged so as to form a regular pentagon. Although, no actual pentagon is present in the figure, we perceive this pentagon due to the corresponding eye movements when transferring our attention from one circle to another. Each movement excites a corresponding *V* , *H* and perhaps *L* center. We do not have however the same sensation, as when the centers of the circles were *actually* connected by straight lines, forming a pentagon. The intensity of excitation of a *V* or *H* center is different for an eye movement following an actual line, from that when the same eye moves over a blank space. In principle this is not surprising. Besides the excitation of the potential eye movement, an actual line produces additional excitation by exciting so many retinal and central neurons. (Rashevsky, 1938, chap. xxvii). The excitation of these neurons may *either enhance or inhibit* the excitation of the corresponding V or H centers, depending on the type of neuronic connections assumed. By studying different theoretically possible cases, we may arrive at a theory of perception and aesthetic values of more general patterns, composed partly of imaginary lines.

6. Effects of associations. It is generally admitted, that any possible *meaning,* associated with a geometric pattern, modifies substantially its aesthetic value. Neurologically this is also to be expected. An "abstract" stimulus pattern produces excitation in a series of centers C (Figure 7), which correspond to its geometrical structure. But if a pattern reminds us of something, or associates with some other previous experience, this means that besides the center C another set of centers C' is excited. If the centers C' are of an excitatory nature, this enhances the total excitation produced by the pattern S, and therefore the aesthetic value of S. But C' may be an inhibitory center, so that its excitation results in an inhibition of other centers. In this case our associations reduce the aesthetic value of the pattern S. It is however possible that even when C' is an inhibiting center, the association results in an increase of the aesthetic value. This may happen, if the "associative fibers", connecting C with C' are very strongly excited and excite, through collaterals, numerous other centers. The total excitation is composed of that of C, C' and the association fibers. These may be so strong, that the net result is an increase of total excitation, even though C' is an inhibitory center.

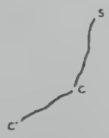

FIGURE 7

These considerations hold quite generally for all types of aesthetic experience. We may enjoy a picture that represents realistically strong human suffering or we enjoy very sad music (Rashevsky, 1938 a, chap. xxx).

Returning again to the aesthetics of visual patterns, we must remember, that a role similar to that of associations, is played by depth and perspective effects. Such effects may also be considered as associational in their nature. Due to the particular arrangement of the elements of the pattern, we see them as arranged in three dimensions, because they produce associations with centers involved in the perception of actual three dimensional figures.

7. Some general expressions. Consider n centers, of which n_1 are excited with an intensity e_1, n_2 with an intensity e_2, etc. We have

$$\sum_i n_i = n. \tag{25}$$

Let each center inhibit every other one with an intensity j_i proportional to its e_i, thus

$$j_i = b_i\, e_i\,. \tag{26}$$

This will be the case, when we neglect the threshold of the inhibitory fibers (Rashevsky, 1938 a, chap. xxii). The more general case of finite thresholds is treated in a similar way.

Each center in the group 1 receives an amount of inhibition: $b_1(n_1 - 1)\,e_1 + b_2 n_2 e_2 + \cdots = \sum_i n_i b_i e_i - b_1 e_1$ and more generally, each center of the group k receives an amount of inhibition equal to

$$\sum_i n_i b_i e_i - b_k e_k.$$

Since there are n_k centers in the k-th group, the total inhibition in that group is $n_k(\sum n_i b_i e_i - b_k e_k)$. The total inhibition is obtained by summing this with respect to k, and because of (25) is equal to

$$J = (n - 1) \sum n_i b_i e_i\,. \tag{27}$$

The *net* excitation is equal to

$$E = \sum n_i e_i - (n - 1) \sum n_i b_i e_i\,. \tag{28}$$

If all b_i have the same value b, equation (28) reduces to

$$E = [1 - (n - 1)\, b] \sum n_i e_i\,. \tag{29}$$

This is the case, considered in *loc. cit.*

When n, which measures the complexity of the pattern, exceeds $(1 + b)/b$, then E becomes negative. This however does not mean that all centers are inhibited, for E gives the *net* excitation. Some centers remain excited, some are inhibited, even when $E < 0$. (Rashevsky, 1938a, chap. xxii). On the other hand, some centers may be already inhibited even when $n < (1 + b)/b$, so that the net value of E is still positive (Rashevsky, 1938 a, chap. xxii).

The excited centers are those, for which $e_k > \sum n_i b_i e_i - b_k e_k$. Since all other centers are inhibited, we arrive at first glance at the absurd conclusion, that some elements of the design, when the latter is too complex, will not be perceived at all. This paradox is resolved however in the following manner: Our attention is concentrated alternately first on those elements of the design, which correspond to the excited centers, then on those which correspond to the inhibited ones. But in this latter case we have to take in the expression for E not the total n, but only the value n^* corresponding to the inhibited elements. This makes n smaller, and reduces the complexity, so that *all* centers now may be excited. In other words, we now break up the very complex pattern in two (or more) partial patterns of lesser complexity, and we either perceive the total pattern as consisting of two or several distinct parts , or as consisting of one outstanding part, seen on a general background.

Such a splitting of a very complex pattern is actually observed on some of the patterns, used by L. Wiley (1940) in his work on evaluation of aesthetic values of abstract designs. For instance in his design No. 9 we definitely see the two block-like figures on a general background of criss-cross lines. Until we have an adequate theory, developed along lines suggested in preceding sections, we cannot predict exactly what part of the design should stand out. Using the crude approximation, adopted in *loc. cit.* and discussed for curves on p. 185 of this paper, however, we find that the strongest excited centers, which would remain uninhibited even if the pattern would be perceived at once, and not in parts, are those corresponding to the lines and angles forming the block-like figure which is seen to stand out on the background of the remaning elements. A similar situation holds for a few other of the complex designs, used by Wiley.

8. Some suggestions for experimental procedure. The final goal of a biophysical theory of visual aesthetics is the theoretical calculations of the aesthetic values of geometric patterns of any complexity and its comparison with psychophysically determined rank order values. However, this goal cannot be reached before all the preliminary work, outlined in this paper has been done. As this work on the partial problems proceeds, experimental verifications should be done all along.

The simplest possible way for such preliminary experiments would be to study first straight lines alone, then angles alone, etc. This cannot be done however, because we cannot perceive an angle without having at least two straight lines to form it. Neither can we have a piece of straight line without ends, the perception of which, as we have seen in section 3, involves some A-centers, the centers involved varying with the position of the straight line in the plane. A compromise method must therefore be adopted.

Having developed a more exact theory of the perception of angles we may verify it by experimenting on different designs, in which lengths and positions of straight lines in the plane do not vary, but angles do. Such is the case with Figures 8a and 8b. For the study of the effects of the *L*-center we may compare designs like those of Figures 8a and 8c, as well as similar polygons of different sizes. In considering similar curvilinear designs, we must remember that an increase in size means a decrease of curvature, and that this may in general affect the intensity in the *A*-centers involved. Having thus definitely established different quantitative aesthetic relations pertaining to angles and lengths, we can use designs involving different *V* and *H* centers. Even if the *L* and *A* centers now vary from design to design, their effect will be known from the preceding study.

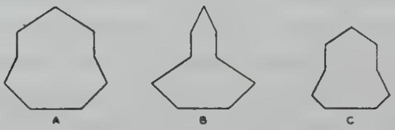

FIGURE 8

A comparison of aesthetic values of designs, consisting of polygons drawn in full lines and similar polygons indicated by dots at their vertices or by some simple pattern, arranged at the vertices, will contribute to the studies discussed in section 6.

As has been stated in *loc. cit.* different parameters entering into our equations and determining the theoretical rank order for a given series of design, vary from individual to individual. This takes into account individual tastes. In actual rank order measurements we determine some sort of average values. Those average values will depend on the distribution function of the different parameters. A theoretical study of the effects of different distributions will form an important problem. With the aid of such studies important conclusions may be drawn from the distribution of individual scores for a given design.

A complete mathematical theory would also indicate to what extent the total aesthetic measure of a design varies with any of the parameters. If a small variation of one of the parameters may result in a large variation of the aesthetic value of the design, we should experiment with designs that are sufficiently different in their aesthetic values. A difference of experimental rank orders 8·5 and 8·4 may be of no use, and either an agreement or disagreement of theory and experiment in such a case may be meaningless. Thus it may be better to use a fewer number of designs spread sufficiently apart, rather than a very large number, forming an almost continuous series. This will also result in a considerable saving of time and labor.

LITERATURE

Householder, A. S. 1939. "A Neural Mechanism for Discrimination." *Psychometrika*, **4**, 45-58.

Householder, A. S. 1940a. "A Neural Mechanism for Discrimination: II. Discrimination of Weights." *Bull. Math. Biophysics*, **2**, 1-13.

Householder, A. S. 1940b. "A Neural Mechanism for Discrimination: III. Visually Perceived Lengths and Distances." *Bull. Math. Biophysics*, **2**, 157-167.

Rashevsky, N. 1938. *Mathematical Biophysics. Physicomathematical Foundations of Biology.* Chicago: The University of Chicago Press.

Rashevsky, N. 1940a. "Contribution to the Mathematical Biophysics of Visual Perception with Special Reference to the Theory of Aesthetic Values of Geometric Patterns." *Psychometrika*, **3**, 253-271.

Rashevsky, N. 1940b. *Advances and Applications of Mathematical Biology.* Chicago: The University of Chicago Press.

Wiley, Llewellyn. 1940. *The Validity of Certain Accepted Criteria of Design.* Thesis. University of Illinois.

INDEX TO VOLUME 4

INDEX OF AUTHORS

PAGE

Bloch, Ingram, and Robert R. Williamson. A Theory of Electrical Polarity in Cells . . . 83

Branson, Herman. Diffusion as a Function of Aggregation in Colloidal Media . . . 1

Branson, Herman. Delayed Adsorption and Diffusion in Colloidal Media . . . 131

Hirsh, Frederick R., Jr. An Explanation of Spastic Walk due to Encephalitis Lethargica . . . 149

Householder, Alston S. A Theory of Steady-State Activity in Nerve-Fiber Networks: IV. *N* Circuits with a Common Synapse . . . 7

Householder, Alston S., and Robert R. Williamson. A Note on the Diffusion of Electrolytes in Cells . . . 73

Householder, Alston S. Cellular Forms: The Tri-Axial Cell . 159

Landahl, H. D. A Kinetic Theory of Diffusion Forces in Metabolizing Systems . . . 15

Landahl, H. D. A Mathematical Analysis of Elongation and Constriction in Cell Division . . . 45

Landahl, H. D. An Expression for the Rate of Return of An Egg after Artificial Deformation . . . 139

Landahl, H. D. An Analysis of the Shapes of a Cell During Division with Particular Reference to the Role of Surface Tension . . . 151

Landahl, H. D. Equilibrium Shapes in Non-Uniform Fields of Concentration . . . 155

Morales, Manuel F., and Nathan W. Shock. A Fundamental Form for the Differential Equation of Colonial and Organism Growth . . . 63

Pitts, Walter. Some Observations on the Simple Neuron Circuit . . . 121

Pitts, Walter. The Linear Theory of Neuron Networks: The Static Problem . . . 169

Rashevsky, N. Suggestions for a Mathematical Biophysics of Auditory Perception with Special Reference to the Theory of Aesthetic Ratings of Combinations of Musical Tones . 27

PAGE

Rashevsky, N. An Alternate Approach to the Mathematical Biophysics of Perception of Combinations of Musical Tones 89
Rashevsky, N. Further Contributions to the Mathematical Biophysics of Visual Aesthetics 117
Rashevsky, N. Some Problems in Mathematical Biophysics of Visual Perception and Aesthetics 177
Sacher, George. Periodic Phenomena in the Interaction of Two Neurons 77
Shock, Nathan W., and Manuel F. Morales. A Fundamental Form for the Differential Equation of Colonial and Organism Growth 63
Stanton, Henry E. A Mathematical Theory of Protoplasmic Protrusions. I. 93
Weinberg, Alvin M. Non-Linear Excitation Theory: Non-Accommodative, Sub-Threshold Effects 33
Weinberg, Alvin M. Green's Functions in Biological Potential Problems 107
Williamson, Robert R., and Alston S. Householder. A Note on the Diffusion of Electrolytes in Cells 73
Williamson, Robert R., and Ingram Bloch. A Theory of Electrical Polarity in Cells 83
Williamson, Robert R. A Theory of Electrical Polarity in Cells: II. 101

INDEX OF SUBJECTS

Adsorption in colloidal media, 131-137
Aesthetic ratings of combinations of musical tones, 27-32
Aesthetics, visual perception and, 177-191
Aggregation in colloidal media, 1-6
Auditory perception, 27-32

Biological potential problems, Green's functions in, 107, 115

Cell division
  constriction in, 45-62
  elongation in, 45-62
  shapes of cell during, 151-154
Cells
  diffusion in, 73-77
  electrical polarity in, 83-88, 101-105
  tri-axial, 159-168
Cellular forms, 159-168
Circuit
  simple neuron, 121-129
  with common synapse, 7-14
Colloidal media, 1-6, 131-137
Colonial and organism growth, 63-71
Combinations of musical tones, 89-90
Concentration, non-uniform fields of, 155-158
Conservation of scholarly journals, 91
Constriction in cell division, 45-62

Deformation, rate of return after, 139-147
Differential equation of colonial and organism, 63-71
Diffusion
  in colloidal media, 1-6, 131-137
  in metabolizing systems, 15-26
  of electrolytes in cells, 73-76
Division
  cell constriction in, 45-62
  cell elongation in, 45-62
  shapes of cell during, 151-154

Egg, rate of return after artificial deformation, 139-147
Electrical polarity in cells, 83-88, 101-105
Electrolytes, diffusion of, 73-76
Elongation in cell division, 45-62
Encephalitis Lethargica, spastic walk due to, 149-150
Equilibrium shapes in non-uniform fields of concentration, 155-158

Fields of concentration, non-uniform, 155-158

Green's functions, 107-115

Interaction of two neurons, 77-81

Kinetic theory of diffusion forces, 15-26

Linear theory of neuron networks, 169-175

Metabolizing systems, 15-26
Musical tones, perception of combinations of, 89-90

Nerve-fiber networks, 7-14
Networks
  nerve-fiber, 7-14
  neuron, 169-175
Neuron
  networks, 169-175
  simple circuit, 121-129
Neurons, interaction of, 77-81
Non-linear excitation theory, 33-44

Perception
  of combinations of musical tones, 89-90
  visual, 177-191
Periodic phenomena, 77-81
Polarity in cells, 83-88, 101-105
Potential problems, biological, 107-115
Protoplasmic protusions, 93-100

Shapes
  in non-uniform fields of concentration, equilibrium, 155-158
  of cell during division, 151-154
Spastic walk due to Encephalitis Lethargica, 149-150
Static problem, 169-175
Steady-state activity of nerve fibers, 7-14
Surface tension, role of during division, 151-154

Visual perception, 177-191

SCOPE OF THE BULLETIN

1. The Bulletin is devoted to publications of research in Mathematical Biophysics, as contributing to the physicomathematical foundations of biology in their most general scope.

2. Papers published in the Bulletin cover physicomathematical theories as well as any other mathematical treatments of biological phenomena, with the exception of purely statistical studies.

3. Mathematical studies in physics or in borderline fields in which a direct connection with biological problems is pointed out are also accepted.

4. Emphasis is put upon the mathematical developments, but a description and discussion of experimental work falls also within the scope of the Bulletin provided that description or discussion is made in close connection with mathematical developments *contained in the same paper.*

5. Outside of the scope of the journal are papers of purely statistical nature or papers concerned only with empirical equations.

PREPARATION OF MANUSCRIPTS

All manuscripts should be typewritten double space. Equations should be numbered on the right consecutively. *Do not* use such notations as "equation 2a" or, "equation 5′" etc. References should be all given at the end of the paper, arranged in alphabetic order by authors and for each author chronologically, following *exactly* the style used in the Bulletin. In text, reference should be made by giving in parentheses the name of the author followed by the year of publication. In case of several publications by the same author in the same year, use notations "1940a", "1940b", etc.

In writing equations, slanted lines should be used wherever possible.

Every paper is to be preceded by a short abstract.

Drawings should be prepared in a professional manner on white paper or tracing cloth following as closely as possible the style used in the Bulletin. They should be drawn approximately twice the scale of the finished reproduction. Lettering should be made by means of a lettering guide. If desired by the authors, drawings may be made at the Editorial Office according to author's instructions, at cost.